EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	322	(562/508).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/11/19 08:47
L3	834	shikimic	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/11/19 08:48
L4	3	l1 and l3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/11/19 08:48
L5	143	dehydroquinase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/11/19 08:48
L6	0	l1 and l5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/11/19 08:48
L7	24	l3 and l5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/11/19 08:49

```
             75 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           1593 REFERENCES IN FILE CAPLUS (1907 TO DATE)
             55 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> e dehyroshikimic acid/cn
E1            1     DEHYQUART SEQ/CN
E2            1     DEHYQUART SP/CN
E3            0 --> DEHYROSHIKIMIC ACID/CN
E4            1     DEHYSAN Z 2226/CN
E5            1     DEHYSOL/CN
E6            1     DEHYSTOLIN/CN
E7            1     DEHYTON AB/CN
E8            1     DEHYTON AB 30/CN
E9            1     DEHYTON AB 40/CN
E10           1     DEHYTON CB/CN
E11           1     DEHYTON G/CN
E12           1     DEHYTON K/CN

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   184.40     184.61

FILE 'REGISTRY' ENTERED AT 06:22:33 ON 19 NOV 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 NOV 2007  HIGHEST RN 954747-20-7
DICTIONARY FILE UPDATES:  18 NOV 2007  HIGHEST RN 954747-20-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d his

     (FILE 'HOME' ENTERED AT 05:57:58 ON 19 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 05:59:50 ON 19 NOV 2007
L1              STRUCTURE UPLOADED
L2            4 SEARCH L1 SSS SAM
L3           67 SEARCH L1 SSS FULL
                SAVE TEMP L3 RWMSTRLST/A
                E SHIKIMIC ACID/CN
L4            1 E3
                E DEHYROSHIKIMIC ACID/CN

     FILE 'REGISTRY' ENTERED AT 06:22:33 ON 19 NOV 2007
```

```
=> l3
SAMPLE SEARCH INITIATED 06:22:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      240 TO ITERATE

100.0% PROCESSED      240 ITERATIONS                                 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          3871 TO     5729
PROJECTED ANSWERS:                4 TO      200

L5            4 SEA SSS SAM L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.45     185.06

FILE 'CAPLUS' ENTERED AT 06:23:22 ON 19 NOV 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Nov 2007  VOL 147 ISS 22
FILE LAST UPDATED: 18 Nov 2007  (20071118/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> l3
L6            17 L3

=> d save temp l6 corehitrefs/a
'TEMP L6 COREHITREFS/A ' IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY SAVED".

=> save temp l6 corehitrefs/a
ANSWER SET L6 HAS BEEN SAVED AS 'COREHITREFS/A'

=> d l6 1-17 ti

L6   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Rational design, synthesis, and evaluation of nanomolar type II
     dehydroquinase inhibitors

L6   ANSWER 2 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Design, synthesis, and structural studies on potent biaryl inhibitors of
     type II dehydroquinases
```

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Determination of the bound conformation of a competitive nanomolar inhibitor of Mycobacterium tuberculosis type II dehydroquinase by NMR spectroscopy

L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar competitive inhibitors of Mycobacterium tuberculosis and Streptomyces coelicolor type II dehydroquinase

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar inhibition of type II dehydroquinase based on the enolate reaction mechanism

L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of inhibitors of type II dehydroquinase and their precursors

L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Crystal Structures of Helicobacter pylori Type II Dehydroquinase Inhibitor Complexes: New Directions for Inhibitor Design

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structure-Based Design, Synthesis, and Biological Evaluation of Inhibitors of Mycobacterium tuberculosis Type II Dehydroquinase

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Hot off the press

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI (1R,4S,5R)-3-Fluoro-1,4,5-trihydroxy-2-cyclohexene-1-carboxylic acid: the fluoro analogue of the enolate intermediate in the reaction catalyzed by type II dehydroquinases

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Parallel Solid-Phase Synthesis and Evaluation of Inhibitors of Streptomyces coelicolor Type II Dehydroquinase

L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Vinyl fluoride as an isoelectronic replacement for an enolate anion: Inhibition of type II dehydroquinases

L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI The Structure and Mechanism of the Type II Dehydroquinase from Streptomyces coelicolor

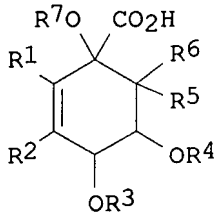
L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Selective Inhibition of Type II Dehydroquinases

L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cyclohexenyl and Cyclohexylidene Inhibitors of 3-Dehydroquinate Synthase: Active Site Interactions Relevant to Enzyme Mechanism and Inhibitor Design

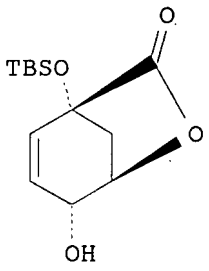
L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis of "iso-EPSP" and evaluation of its interaction with chorismate synthase

=> resin

```
       648554 RESIN
       423593 RESINS
L7     794031 RESIN
                (RESIN OR RESINS)

=> l6 and l7
L8          3 L6 AND L7

=> d l8 1-3 ti fbib abs

L8   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of inhibitors of type II dehydroquinase and their precursors
AN   2006:277621  CAPLUS
DN   144:274493
TI   Preparation of inhibitors of type II dehydroquinase and their precursors
IN   Gonzalez Bello, Concepcion; Castedo Exposito, Luis
PA   Universidade de Santiago de Compostela, Spain
SO   Span., 24 pp.
     CODEN: SPXXAD
DT   Patent
LA   Spanish
FAN.CNT 2
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ---------------     ----   --------    ---------------------    --------
PI   ES 2223284          A1     20050216    ES 2003-1709             20030721
     ES 2223284          B2     20060101
     EP 1647544          A2     20060419    EP 2004-742065           20040716
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
                                             ES 2003-1709         A  20030721
                                             WO 2004-ES337        W  20040716
     US 2007185214       A1     20070809    US 2006-565348           20060802
                                             ES 2003-1709         A  20030721
                                             WO 2004-ES337        W  20040716

PATENT FAMILY INFORMATION:
FAN  2005:99298
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ---------------     ----   --------    ---------------------    --------
PI   WO 2005009330       A2     20050203    WO 2004-ES337            20040716
     WO 2005009330       A3     20050317
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
                                             ES 2003-3001709      A  20030721
     EP 1647544          A2     20060419    EP 2004-742065           20040716
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
                                             ES 2003-1709         A  20030721
                                             WO 2004-ES337        W  20040716
     US 2007185214       A1     20070809    US 2006-565348           20060802
                                             ES 2003-1709         A  20030721
                                             WO 2004-ES337        W  20040716
OS   CASREACT 144:274493; MARPAT 144:274493
GI
```



I



II

AB The invention relates to type II dehydroquinase inhibitors having carboxycyclohexene structure I [R1-7 are H, acyloxy, alkoxy, aryloxy, alkylthio, alkylamino, alkylazido, alkylphosphate, alkylcarboxy, arylthio, alkyl, (un)substituted benzyloxy, etc.], including their synthesis from (-)-quinic acid and use as antitumor, antimicrobial, immunosuppressive or herbicidal agents. Thus, lactone II (TBS = tert-butyldimethylsilyl) was attached to a BromoWang resin, the TBS group cleaved (Bu4NF), the hydroxyl group benzylated, and the resin cleaved (TFA) to afford (R,R,R)-I (R1-R6 = H, R7 = PhCH2).

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors
AN 2005:99298 CAPLUS
DN 142:172177
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors
IN Gonzalez Bello, Concepcion; Castedo Expostio, Luis
PA Universidade De Santiago De Compostela, Spain
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005009330	A2	20050203	WO 2004-ES337	20040716
WO 2005009330	A3	20050317		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			ES 2003-3001709	A 20030721
EP 1647544	A2	20060419	EP 2004-742065	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
			ES 2003-1709	A 20030721
			WO 2004-ES337	W 20040716
US 2007185214	A1	20070809	US 2006-565348	20060802
			ES 2003-1709	A 20030721
			WO 2004-ES337	W 20040716

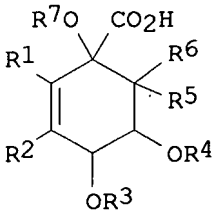
PATENT FAMILY INFORMATION:

FAN 2006:277621

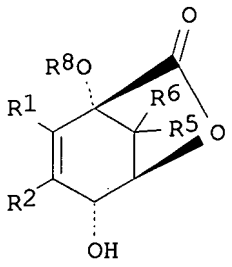
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	ES 2223284	A1	20050216	ES 2003-1709	20030721
	ES 2223284	B2	20060101		
	EP 1647544	A2	20060419	EP 2004-742065	20040716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
				ES 2003-1709 A	20030721
				WO 2004-ES337 W	20040716
	US 2007185214	A1	20070809	US 2006-565348	20060802
				ES 2003-1709 A	20030721
				WO 2004-ES337 W	20040716

OS MARPAT 142:172177

GI



I



II

AB The invention relates to type II dehydroquinase inhibitors having a carboxycyclohexene structure I (R1-7 = H, C1-10-acyloxy, -alkyloxy, -aryloxy-, -alkylthio, -alkylamino, -alkylnitro, -alkylazido, -alkylphosphate, -alkylcarboxy, -arylthio, (substituted)benzyloxy, etc.). Also disclosed is a method of obtaining I from II (R1,R2,R5,R6 = same as in I; R8 = protecting group) by alkylation of the free hydroxyl, removal of R8, alkylation of the newly exposed hydroxyl group, removal of the first alkyl group and hydrolysis of the lactone followed by modification of the two hydroxy groups. I may be used as antitumor, antimicrobial, and immunosuppressive agents and as herbicides.

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

TI Parallel Solid-Phase Synthesis and Evaluation of Inhibitors of Streptomyces coelicolor Type II Dehydroquinase

AN 2003:921939 CAPLUS

DN 140:76845

TI Parallel Solid-Phase Synthesis and Evaluation of Inhibitors of Streptomyces coelicolor Type II Dehydroquinase

AU Gonzalez-Bello, Concepcion; Lence, Emilio; Toscano, Miguel D.; Castedo, Luis; Coggins, John R.; Abell, Chris

CS Departamento de Quimica Organica y Unidad Asociada al C.S.I.C., Facultad de Quimica, Universidad de Santiago de Compostela, Santiago de Compostela, 15782, Spain

SO Journal of Medicinal Chemistry (2003), 46(26), 5735-5744
CODEN: JMCMAR; ISSN: 0022-2623

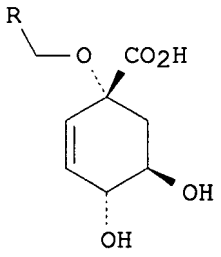
PB American Chemical Society

DT Journal

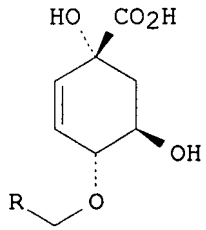
LA English

OS CASREACT 140:76845

GI



I



II

AB A series of cyclohexenecarboxylic acids I (R = Ph, 4-FC6H4, 4-HO2CC6H4, 2-O2NC6H4, etc.) and II, which are 1-substituted and 4-substituted benzyl analogs of the known inhibitor (1S,3R,4R)-1,3,4-trihydroxy-5-cyclohexene-1-carboxylic acid, has been synthesized using solid-phase approach, and these compds. were tested as inhibitors of Streptomyces coelicolor type II dehydroquinase. The most potent inhibitor, II (R = 2-O2NC6H4), has Ki of 8 μM, more than 30 times lower than the KM of the substrate and approx. 4 times more potent than the original inhibitor. The binding modes of I and II in the active site were studied by mol. docking with GOLD 2.0.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l6 15 ti fbib abs

L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Selective Inhibition of Type II Dehydroquinases
AN 1999:199491 CAPLUS
DN 131:29204
TI Selective Inhibition of Type II Dehydroquinases
AU Frederickson, Martyn; Parker, Emily J.; Hawkins, Alastair R.; Coggins, John R.; Abell, Chris
CS University Chemical Laboratory, Cambridge, CB2 1EW, UK
SO Journal of Organic Chemistry (1999), 64(8), 2612-2613
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
AB Four analogs of the proposed enolate intermediate of dehydroquinase (3-dehydroquinate dehydratase) were prepared The analogs were assayed for their inhibitory properties against type I and type II dehydroquinases. All of the inhibitors showed inhibition of both type I and II dehydroquinases. Two inhibitors were clearly selective for type II dehydroquinases and exhibited unexpected discrimination between different type II enzymes. All the compds. were poor inhibitors against the type I enzyme. The results are encouraging and suggest that compds. combining the sep. strategies of flattening the ring and having a hydrogen-bonding capability at C-3 should be interesting targets.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l6 14,16,17 ti fbib abs

L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI The Structure and Mechanism of the Type II Dehydroquinase from Streptomyces coelicolor
AN 2002:264848 CAPLUS
DN 137:29785
TI The Structure and Mechanism of the Type II Dehydroquinase from

Streptomyces coelicolor
AU Roszak, Aleksander W.; Robinson, David A.; Krell, Tino; Hunter, Iain S.; Fredrickson, Martyn; Abell, Chris; Coggins, John R.; Lapthorn, Adrian J.
CS Department of Chemistry, Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK
SO Structure (Cambridge, MA, United States) (2002), 10(4), 493-503
CODEN: STRUE6; ISSN: 0969-2126
PB Cell Press
DT Journal
LA English
AB The structure of the type II DHQase from Streptomyces coelicolor has been solved and refined to high resolution in complexes with a number of ligands, including dehydroshikimate and a rationally designed transition state analog, 2,3-anhydro-quinic acid. These structures define the active site of the enzyme and the role of key amino acid residues and provide snap shots of the catalytic cycle. The resolution of the flexible lid domain (residues 21-31) shows that the invariant residues Arg23 and Tyr28 close over the active site cleft. The tyrosine acts as the base in the initial proton abstraction, and evidence is provided that the reaction proceeds via an enol intermediate. The active site of the structure of DHQase in complex with the transition state analog also includes mols. of tartrate and glycerol, which provide a basis for further inhibitor design.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cyclohexenyl and Cyclohexylidene Inhibitors of 3-Dehydroquinate Synthase: Active Site Interactions Relevant to Enzyme Mechanism and Inhibitor Design
AN 1997:528717 CAPLUS
DN 127:216861
TI Cyclohexenyl and Cyclohexylidene Inhibitors of 3-Dehydroquinate Synthase: Active Site Interactions Relevant to Enzyme Mechanism and Inhibitor Design
AU Montchamp, Jean-Luc; Frost, J. W.
CS Contribution from the Department of Chemistry, Michigan State University, East Lansing, MI, 48824, USA
SO Journal of the American Chemical Society (1997), 119(33), 7645-7653
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB Cyclohexenyl and cyclohexylidene inhibitors possessing strategically placed olefinic residues, in general, bind to 3-dehydroquinate (DHQ) synthase more tightly than similarly substituted cyclohexyl inhibitors. All of the newly synthesized inhibitors were prepared from a common DHQ derivative Cyclohexenyl phosphate 1 is the most potent inhibitor of DHQ synthase thus far identified with an inhibition constant (Ki = 1.2+10-10 M), indicating active site binding 1000-fold tighter relative to the corresponding cyclohexyl phosphate 5. Cyclohexenyl tricarboxylate 2 binds 700-fold more tightly than similarly substituted cyclohexyl tricarboxylate 6 and is the first example of a nanomolar-level inhibitor (Ki = 8.6+10-9 M) possessing neither a phosphate monoester or a phosphonic acid. Cyclohexenyl homophosphonate 4 (Ki = 3.0+10-8 M) and cyclohexylidene homophosphonate 10 (Ki = 3.2+10-9 M) bind 57- and 530-fold, resp., more tightly than the corresponding cyclohexyl homophosphonate 8. Cyclohexylidene homophosphonate 10 is the first example of a nanomolar-level, homophosphonic acid inhibitor of DHQ synthase. Cyclohexylidene phosphonate 9 (Ki = 2.9+10-10 M) is a 2.9-fold more potent inhibitor relative to cyclohexyl phosphonate 7 which was previously the most potent, slowly-reversible inhibitor of DHQ synthase. Cyclohexenyl phosphonate 3 (Ki = 1.2+10-9 M) is the only olefin-containing, carbocyclic inhibitor where improved binding over the corresponding cyclohexyl analog was not observed The impact of olefinic residues in inhibitors on active site binding may indicate that DHQ

synthase plays an active catalytic role during E1cb elimination of inorg. phosphate from enzyme-bound substrate.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis of "iso-EPSP" and evaluation of its interaction with chorismate synthase
AN 1987:2165 CAPLUS
DN 106:2165
TI Synthesis of "iso-EPSP" and evaluation of its interaction with chorismate synthase
AU Bartlett, Paul A.; Maitra, Uday; Chouinard, Paul M.
CS Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
SO Journal of the American Chemical Society (1986), 108(25), 8068-71
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB The allylic phosphate isomer (iso-EPSP) of 5-enol-pyruvylshikimate 3-phosphate (EPSP) was synthesized starting with (-)-quinic acid. Iso-EPSP was not an alternative substrate for chorismate synthase isolated from Neurospora crassa, although it was a good inhibitor (Ki = 8.7 μM). Apparently, the enzymic conversion of EPSP to chorismate does not involve allylic rearrangement followed by 1,2-elimination.

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	52.78	237.84
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-5.46

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 06:37:36 ON 19 NOV 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 07:22:25 ON 19 NOV 2007
FILE 'CAPLUS' ENTERED AT 07:22:25 ON 19 NOV 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	52.78	237.84
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-5.46

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	53.25	238.31

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-5.46

FILE 'REGISTRY' ENTERED AT 07:22:49 ON 19 NOV 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 NOV 2007 HIGHEST RN 954747-20-7
DICTIONARY FILE UPDATES: 18 NOV 2007 HIGHEST RN 954747-20-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

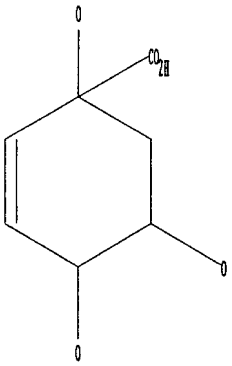
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

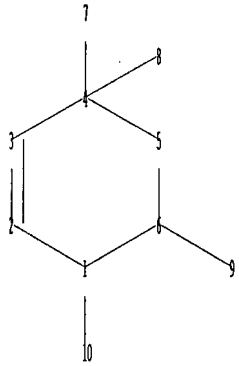
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

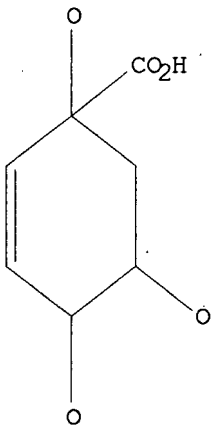
=>
Uploading C:\Documents and Settings\PZucker\My Documents\Examination Auxillary files\10565348\10565348 broader core structure.str





chain nodes :
7 8 9 10
ring nodes :
1 2 3 4 5 6
chain bonds :
1-10 4-7 4-8 6-9
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 1-10 2-3 3-4 4-5 4-7 5-6 6-9
exact bonds :
4-8

```
Hydrogen count :
1:>= minimum 1  6:>= minimum 1
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS



L9      STRUCTURE UPLOADED

=> d l9
L9 HAS NO ANSWERS
L9              STR
```




```
Structure attributes must be viewed using STN Express query preparation.


=> search l9 sss sam
SAMPLE SEARCH INITIATED 07:23:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      240 TO ITERATE

100.0% PROCESSED     240 ITERATIONS                                  4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3871 TO     5729
PROJECTED ANSWERS:               4 TO      200

L10           4 SEA SSS SAM L9

=> search l9 sss full
FULL SEARCH INITIATED 07:23:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     4630 TO ITERATE

100.0% PROCESSED     4630 ITERATIONS                                 67 ANSWERS
SEARCH TIME: 00.00.01

L11          67 SEA SSS FUL L9

=> save temp l11 superset/a
ANSWER SET L11 HAS BEEN SAVED AS 'SUPERSET/A'

=> logof hold
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
```

	ENTRY	SESSION
FULL ESTIMATED COST	172.55	410.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-5.46

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 07:24:11 ON 19 NOV 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 07:30:13 ON 19 NOV 2007
FILE 'REGISTRY' ENTERED AT 07:30:13 ON 19 NOV 2007
COPYRIGHT (C) 2007 American Chemical Society (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.55	410.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-5.46

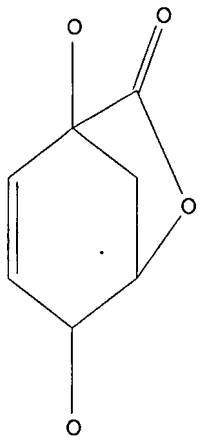
=>
Uploading C:\Documents and Settings\PZucker\My Documents\Examination Auxillary files\10565348\10565348 lactone core structure.str

chain nodes :
7 10 12
ring nodes :
1 2 3 4 5 6 8 9
chain bonds :
1-10 4-7 8-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-8 5-6 6-9 8-9
exact/norm bonds :
1-2 1-6 1-10 2-3 3-4 4-5 4-7 4-8 5-6 6-9 8-9 8-12

Hydrogen count :
1:>= minimum 1 6:>= minimum 1
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 12:CLASS

L12   STRUCTURE UPLOADED

=> d l12
L12 HAS NO ANSWERS
L12   STR



Structure attributes must be viewed using STN Express query preparation.

=> d his

     (FILE 'HOME' ENTERED AT 05:57:58 ON 19 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 05:59:50 ON 19 NOV 2007
L1   STRUCTURE UPLOADED
L2   4 SEARCH L1 SSS SAM
L3   67 SEARCH L1 SSS FULL
               SAVE TEMP L3 RWMSTRLST/A
               E SHIKIMIC ACID/CN
L4   1 E3
               E DEHYROSHIKIMIC ACID/CN

     FILE 'REGISTRY' ENTERED AT 06:22:33 ON 19 NOV 2007
L5   4 L3

     FILE 'CAPLUS' ENTERED AT 06:23:22 ON 19 NOV 2007
L6   17 L3
               SAVE TEMP L6 COREHITREFS/A
L7   794031 RESIN
L8   3 L6 AND L7

     FILE 'REGISTRY' ENTERED AT 07:22:49 ON 19 NOV 2007
L9   STRUCTURE UPLOADED
L10   4 SEARCH L9 SSS SAM
L11   67 SEARCH L9 SSS FULL
               SAVE TEMP L11 SUPERSET/A
L12   STRUCTURE UPLOADED

```
=> search l12 subset=l11 sss sam
SAMPLE SUBSET SEARCH INITIATED 07:35:01 FILE 'REGISTRY'
SAMPLE SUBSET SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                 0 ANSWERS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET):           ONLINE  **COMPLETE**
PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET):          0 TO        0
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):             0 TO        0

L13           0 SEA SUB=L11 SSS SAM L12

=> search l12 subset=l11 sss full
FULL SUBSET SEARCH INITIATED 07:35:10 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                 0 ANSWERS
SEARCH TIME: 00.00.01

L14           0 SEA SUB=L11 SSS FUL L12

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                              219.95     458.26

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00      -5.46

FILE 'CAPLUS' ENTERED AT 07:39:09 ON 19 NOV 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Nov 2007  VOL 147 ISS 22
FILE LAST UPDATED: 18 Nov 2007  (20071118/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> l3/thu
            17 L3
        954677 THU/RL
L15          7 L3/THU
                 (L3 (L) THU/RL)

=> d l15 1-7 ti
```

L15 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Rational design, synthesis, and evaluation of nanomolar type II dehydroquinase inhibitors

L15 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Design, synthesis, and structural studies on potent biaryl inhibitors of type II dehydroquinases

L15 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Determination of the bound conformation of a competitive nanomolar inhibitor of Mycobacterium tuberculosis type II dehydroquinase by NMR spectroscopy

L15 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar competitive inhibitors of Mycobacterium tuberculosis and Streptomyces coelicolor type II dehydroquinase

L15 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar inhibition of type II dehydroquinase based on the enolate reaction mechanism

L15 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of inhibitors of type II dehydroquinase and their precursors

L15 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors

=> d l15 7 ti fbib abs

L15 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors
AN 2005:99298 CAPLUS
DN 142:172177
TI Inhibitors of type II dehydroquinase, methods for their synthesis, and their use as herbicides, antitumor and antimicrobial agents, and tumor suppressors
IN Gonzalez Bello, Concepcion; Castedo Expostio, Luis
PA Universidade De Santiago De Compostela, Spain
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005009330	A2	20050203	WO 2004-ES337	20040716
	WO 2005009330	A3	20050317		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

				ES 2003-3001709	A 20030721
EP 1647544		A2	20060419	EP 2004-742065	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
				ES 2003-1709	A 20030721
				WO 2004-ES337	W 20040716
US 2007185214		A1	20070809	US 2006-565348	20060802
				ES 2003-1709	A 20030721
				WO 2004-ES337	W 20040716

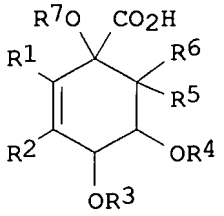
PATENT FAMILY INFORMATION:

FAN 2006:277621

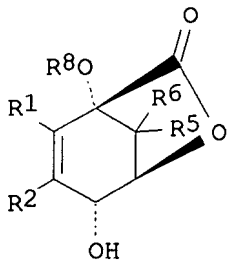
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ES 2223284	A1	20050216	ES 2003-1709	20030721
ES 2223284	B2	20060101		
EP 1647544	A2	20060419	EP 2004-742065	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
			ES 2003-1709	A 20030721
			WO 2004-ES337	W 20040716
US 2007185214	A1	20070809	US 2006-565348	20060802
			ES 2003-1709	A 20030721
			WO 2004-ES337	W 20040716

OS MARPAT 142:172177

GI



I



II

AB The invention relates to type II dehydroquinase inhibitors having a carboxycyclohexene structure I (R1-7 = H, C1-10-acyloxy, -alkyloxy, -aryloxy-, -alkylthio, -alkylamino, -alkylnitro, -alkylazido, -alkylphosphate, -alkylcarboxy, -arylthio, (substituted)benzyloxy, etc.). Also disclosed is a method of obtaining I from II (R1,R2,R5,R6 = same as in I; R8 = protecting group) by alkylation of the free hydroxyl, removal of R8, alkylation of the newly exposed hydroxyl group, removal of the first alkyl group and hydrolysis of the lactone followed by modification of the two hydroxy groups. I may be used as antitumor, antimicrobial, and immunosuppressive agents and as herbicides.

=> d l15 1-6 ti fbib abs

L15 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

TI Rational design, synthesis, and evaluation of nanomolar type II dehydroquinase inhibitors

AN 2007:808773 CAPLUS

DN 147:268289

TI Rational design, synthesis, and evaluation of nanomolar type II dehydroquinase inhibitors

AU Payne, Richard J.; Peyrot, Fabienne; Kerbarh, Olivier; Abell, Andrew D.; Abell, Chris

CS Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK
SO ChemMedChem (2007), 2(7), 1015-1029
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB The in silico design, synthesis, and biol. evaluation of ten potent type II dehydroquinase inhibitors are described. These compds. contain an anhydroquinate core, incorporated as a mimic of the enolate reaction intermediate. This substructure is attached by a variety of linking units to a terminal Ph group that binds in an adjacent pocket. Inhibitors were synthesized from (-)-quinic acid using palladium-catalyzed Stille and carboamidation chemical Several inhibitors exhibited nanomolar inhibition consts. against type II dehydroquinases from Streptomyces coelicolor and Mycobacterium tuberculosis. These are among the most potent inhibitors of these enzymes reported to date.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

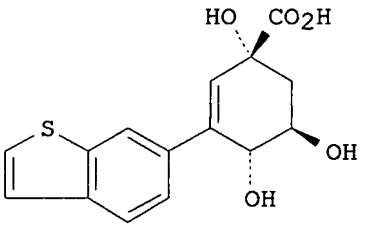
L15 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Design, synthesis, and structural studies on potent biaryl inhibitors of type II dehydroquinases
AN 2007:808772 CAPLUS
DN 147:335606
TI Design, synthesis, and structural studies on potent biaryl inhibitors of type II dehydroquinases
AU Payne, Richard J.; Riboldi-Tunnicliffe, Alan; Kerbarh, Olivier; Abell, Andrew D.; Lapthorn, Adrian J.; Abell, Chris
CS Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK
SO ChemMedChem (2007), 2(7), 1010-1013
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB Using docking studies and mol. modeling, new antibacterial derivs. of an anhydroquinate were synthesized and tested.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Determination of the bound conformation of a competitive nanomolar inhibitor of Mycobacterium tuberculosis type II dehydroquinase by NMR spectroscopy
AN 2007:344599 CAPLUS
DN 147:856
TI Determination of the bound conformation of a competitive nanomolar inhibitor of Mycobacterium tuberculosis type II dehydroquinase by NMR spectroscopy
AU Prazeres, Veronica F. V.; Sanchez-Sixto, Cristina; Castedo, Luis; Canales, Angeles; Canada, Francisco Javier; Jimenez-Barbero, Jesus; Lamb, Heather; Hawkins, Alastair R.; Gonzalez-Bello, Concepcion
CS Laboratorio de Quimica Organica CSIC and Departamento de Quimica Organica Facultad de Quimica, Universidad de Santiago de Compostela, Santiago de Compostela, 15782, Spain
SO ChemMedChem (2006), 1(9), 990-996
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB The synergy between tuberculosis and the AIDS epidemic, along with the surge of multidrug-resistant isolates of M. tuberculosis, has reaffirmed tuberculosis as a primary public health threat. It is therefore necessary to discover new, safe, and more efficient antibiotics against this

disease. On the other hand, mapping the dynamic interactions of inhibitors of a target protein can provide information for the development of more potent inhibitors and consequently, more potent potential drugs. In this context, the conformational binding of our previously reported nanomolar inhibitor of M. tuberculosis type II dehydroquinase, the 3-nitrophenyl derivative 1, was studied using saturation transfer difference (STD) and transferred NOESY expts. These studies have shown that in the bound state, one conformation of those present in solution of the competitive nanomolar inhibitor 3-nitrophenyl derivative 1 is selected. In the bound conformation, the aromatic ring is slightly shifted from coplanarity, with the double bond and the nitro group of 1 oriented towards the double bond side.

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar competitive inhibitors of Mycobacterium tuberculosis and Streptomyces coelicolor type II dehydroquinase
AN 2007:341066 CAPLUS
DN 147:673
TI Nanomolar competitive inhibitors of Mycobacterium tuberculosis and Streptomyces coelicolor type II dehydroquinase
AU Prazeres, Veronica F. V.; Sanchez-Sixto, Cristina; Castedo, Luis; Lamb, Heather; Hawkins, Alastair R.; Riboldi-Tunnicliffe, Alan; Coggins, John R.; Lapthorn, Adrian J.; Gonzalez-Bello, Concepcion
CS Laboratorio de Quimica Organica, CSIC and Departamento de Quimica Organica Facultad de Quimica, Universidad de Santiago de Compostela, Santiago de Compostela, 15782, Spain
SO ChemMedChem (2007), 2(2), 194-207
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
GI



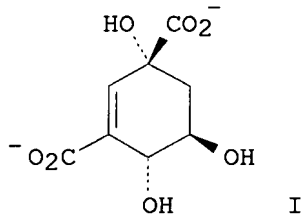
I

AB Isomeric nitrophenyl and heterocyclic analogs of the known inhibitor (1S,3R,4R)-1,3,4-trihydroxy-5-cyclohexene-1-carboxylic acid have been synthesized and tested as inhibitors of M. tuberculosis and S. coelicolor type II dehydroquinase, the third enzyme of the shikimic acid pathway. The target compds. were synthesized by a combination of Suzuki and Sonogashira cross-coupling and copper(I)-catalyzed 2,3-dipolar cycloaddn. reactions from a common vinyl triflate intermediate. These studies showed that a para-nitrophenyl derivative is almost 20-fold more potent as a competitive inhibitor against the S. coelicolor enzyme than that of M. tuberculosis. The opposite results were obtained with the meta isomer. Five of the bicyclic analogs reported herein proved to be potent competitive inhibitors of S. coelicolor dehydroquinase, with inhibition consts. in the low nanomolar range (4-30 nM). These derivs. are also competitive inhibitors of the M. tuberculosis enzyme, but with lower affinities. The most potent inhibitor against the S. coelicolor enzyme, a

6-benzothiophenyl derivative (I), has a Ki value of 4 nM-over 2000-fold more potent than the best previously known inhibitor, (1R,4R,5R)-1,5-dihydroxy-4-(2-nitrophenyl)cyclohex-2-en-1-carboxylic acid (8 μM), making it the most potent known inhibitor against any dehydroquinase. The binding modes of the analogs in the active site of the S. coelicolor enzyme (GOLD 3.0.1), suggest a key π-stacking interaction between the aromatic rings and Tyr 28, a residue that has been identified as essential for enzyme activity.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Nanomolar inhibition of type II dehydroquinase based on the enolate reaction mechanism
AN 2007:341043 CAPLUS
DN 147:671
TI Nanomolar inhibition of type II dehydroquinase based on the enolate reaction mechanism
AU Toscano, Miguel D.; Payne, Richard J.; Chiba, Akira; Kerbarh, Olivier; Abell, Chris
CS Department of Chemistry, University Chemical Laboratory, University of Cambridge, Cambridge, CB2 1EW, UK
SO ChemMedChem (2007), 2(1), 101-112
CODEN: CHEMGX; ISSN: 1860-7179
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 147:671
GI



I

AB The authors describe the rational design of a novel, highly potent inhibitor of type II dehydroquinase, the dicarboxylate (I). The incorporation of a carboxylate at the 3-position mimics the putative enolate intermediate in the reaction mechanism, and allows a potential electrostatic binding interaction with the arginine on the active site flap. This results in a 1000-fold increase in potency, making the dicarboxylate I the most potent inhibitor of type II dehydroquinase reported to date, with a high ligand efficiency of -0.68 kcal mol-1 per nonhydrogen atom. The systematic dissection of I in compds. 7-12, all of which show a drop in potency, confirm the synergistic importance of the two carboxylates, the C3 and C4 hydroxyl groups, and the anhydroquinate ring structure for the potency of I.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of inhibitors of type II dehydroquinase and their precursors
AN 2006:277621 CAPLUS
DN 144:274493
TI Preparation of inhibitors of type II dehydroquinase and their precursors
IN Gonzalez Bello, Concepcion; Castedo Exposito, Luis

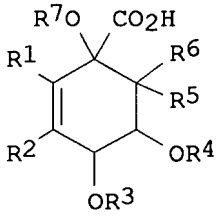
PA Universidade de Santiago de Compostela, Spain
SO Span., 24 pp.
CODEN: SPXXAD
DT Patent
LA Spanish
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ES 2223284	A1	20050216	ES 2003-1709	20030721
ES 2223284	B2	20060101		
EP 1647544	A2	20060419	EP 2004-742065	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
			ES 2003-1709 A	20030721
			WO 2004-ES337 W	20040716
US 2007185214	A1	20070809	US 2006-565348	20060802
			ES 2003-1709 A	20030721
			WO 2004-ES337 W	20040716

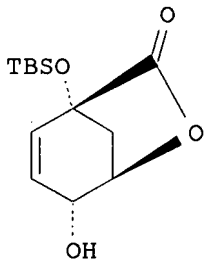
PATENT FAMILY INFORMATION:
FAN 2005:99298

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005009330	A2	20050203	WO 2004-ES337	20040716
WO 2005009330	A3	20050317		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			ES 2003-3001709 A	20030721
EP 1647544	A2	20060419	EP 2004-742065	20040716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
			ES 2003-1709 A	20030721
			WO 2004-ES337 W	20040716
US 2007185214	A1	20070809	US 2006-565348	20060802
			ES 2003-1709 A	20030721
			WO 2004-ES337 W	20040716

OS CASREACT 144:274493; MARPAT 144:274493
GI



I



II

AB The invention relates to type II dehydroquinase inhibitors having carboxycyclohexene structure I [R1-7 are H, acyloxy, alkoxy, aryloxy, alkylthio, alkylamino, alkylazido, alkylphosphate, alkylcarboxy, arylthio,

alkyl, (un)substituted benzyloxy, etc.], including their synthesis from (-)-quinic acid and use as antitumor, antimicrobial, immunosuppressive or herbicidal agents. Thus, lactone II (TBS = tert-butyldimethylsilyl) was attached to a BromoWang resin, the TBS group cleaved (Bu4NF), the hydroxyl group benzylated, and the resin cleaved (TFA) to afford (R,R,R)-I (R1-R6 = H, R7 = PhCH2).

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	39.98	498.24

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-10.92

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 07:41:38 ON 19 NOV 2007